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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHANNAVAJJALA, LAKSHMI SARADA	

ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
08/04/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)
	09/553,969	WALLACE ET AL.
	Examiner	Art Unit
	LAKSHMI CHANNAVAJJALA	1611

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 May 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,19,21,24,30-32 and 34-63* is/are pending in the application.

4a) Of the above claim(s) *37-63* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,19,21,24,30-32 and 34-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)	
1) ☐ Notice of References Cited (PTO-892)	4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) ☐ Notice of Informal Patent Application
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/14/11 and 5/19/11*.	6) ☐ Other: _____.

DETAILED ACTION

Receipt of amendment and response dated 5/13/11; and IDS dated 3/14/11 and 5/19/11 is acknowledged.

Claims 1, 19, 21, 24, 30-32 and 34-63 are pending. Claims 2-18, 20, 22-23 and 25-29 have been canceled. Claims 37-63 have been withdrawn.

Applicants submit that the present amendments do not require the non-cross-linked polymeric material and hence are similar to the claims as previously pending prior to the Amendment filed February 25, 2010.

In light of the above submission and cancellation of the claim limitations that require non-crosslinked gelatin polymer & the introduction of new limitation that the single phase aqueous colloid is partially hydrated with an aqueous medium, the examiner has withdrawn the pending rejection of record and the following rejection previously of record (prior to the amendment of 2/25/10) has been presented:

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

1. **Claims 1, 19, 21 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,482,386 to Wittwer et al (Wittwer) in view of US 4,124,705 to Rothman et al and US 4,515,637 to Cioca**.

Wittwer et al teaches conditioned water-swellable hydrocolloids for use in mechanical forming processes such as processes die molding or injection molding in preparing shaped articles (abstract, col. 10 and col. 2, L 66 through col. 3, l 13). Wittwer teaches a number of polymers such as protein or non-biological polymers for preparing swellable hydrocolloids including gelatin (col. 2, L 37-57).

Example in col. 4 describes gelatin preparation, where in gelatin is conditioned or hydrated to 15% water content and the gelating granules, which reads on the "partially hydrated colloid." Further, Wittwer teaches that gelatin is in a granulated form with a mean particle diameter of 0.2 to 4 mm. (claim 6 of the patent). With respect to the degradation claimed, the property of degradation is associated with gelatin. With respect to the claimed "equilibrium swell", instant specification describes that the equilibrium swell ranging from 400% to 5000% may be controlled by varying the degree of cross-linking, which in turn is achieved by varying the cross-linking conditions, such as the type of cross-linking method, duration of exposure of a cross-linking agent, concentration of a cross-linking agent, cross-linking temperature, and the like. Wittwer does not teach the hydrocolloid in an applicator but suggests that the granulated gelatin is coupled with a molding unit such as an injection molding machine and therefore the claimed hydrogel being in an applicator with an extrusion orifice so as to be able to inject gelatin hydrocolloid would have been within the scope of a skilled artisan.

In this regard, Wittwer teaches crosslinking of the hydrocolloid polymers is carried out with known cross-linking agents such as aldehydes, salts etc., to control water swellability (col.2, l 49-60). Examiner further notes that the instant examples

describe glutaraldehyde cross-linking gelatin to achieve the equilibrium swell. Even though Wittwer fails to exemplify other swellable polymers, it would have been obvious for a skilled artisan to choose a biological polymer such as protein or a non-biological polymer or a synthetic polymer and crosslink the same employing known crosslinking agents so as to prepare swellable hydrocolloids because Wittwer suggests that the process of preparing a swellable hydrocolloids of predetermined water content, that are suitable for preparing moldable or shaped articles can also be prepared with synthetic polymers.

Wittwer fails to teach an active agent (claim 25) such as a clotting agent (claim 26) or thrombin.

Rothman et al (hereafter Rothman) discloses an agent for intravascular administration consisting of a suspension of minute particles of a polysaccharide that is blocks the finer blood vessels (abstract, lines bridging col. 1-2 and paragraph bridging col. 11-col. 12). The polysaccharide of Rothman is biodegradable and resorbable because Rothman describes that the hydrophilic swellable particles are broken down by alpha-amylase in the blood plasma (col. 2, l 4-16) and further, according to the instant claim 35, the ability to be resorbable is inherent to the polysaccharide of Rothman. Similarly, the ability to swell is a property inherent to the polysaccharides described by Rothman. Rothman teaches a size range of 0.1 to 300 microns (col. 5, L 18-36), which overlaps with the claimed range of 0.01 mm to 5 mm (10 microns-5000 microns). Rothman further describes that the polymeric gel particles are produced by disintegrating the larger pieces of gel, which reads on fragmented gel claimed in the

instant (col. 8, L 3-14). With respect to the limitations of "single phase" and "substantially free form a free aqueous phase", Rothman does not teach including any other substance or component in the polysaccharide suspension other than for the formation of the gel or the ability to form a gel, and also states that the gels contain more than 50% by weight water but less than 98%water (col. 4, L 58-70), which implies that the gels do not contain any free water. Rothman discloses that the particulate suspension is injected intravascularly (col. 8, L 31-48), in conjunction with a therapeutic (col. 9, L 25-34) or a diagnostic agent (col. 8, L 49 through col. 9, L 24). Further the particulate suspension containing polysaccharide particles (of Rothman) read on a single phase aqueous colloid and are swellable upon administration and hence the presence of aqueous solution (for suspending the particles) and hence read on the claimed "free from a free aqueous phase". The therapeutic or diagnostic agents of Rothman read on instant claim 25 and particularly mention coagulation factors of claim 26 (col. 9, line 28-30). Rothman fails to teach the specific clotting agent, thrombin of claim 27, but teaches inclusion of clotting agents in the swellable gels for affecting coagulation.

Cioca teaches thrombin as an effective clotting factor for stoppage of bleeding locally (col. 2). Therefore, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention was made to use swellable hydrocolloids of Wittwer containing gelatin polymer for delivering active agents such as coagulating factors to the desired site because Rothman suggests swellable hydrogels for delivering therapeutic agents such as coagulating agents. Further, it would have been obvious for

a skilled artisan to include thrombin as a coagulation factor in the hydrogel composition of Wittwer with an expectation of achieving the desired clotting or coagulation.

2. Claims 30-32 and 35-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4482386 to Wittwer) in view of US 4,124,705 to Rothman et al and US 4,515,637 to Cioca as applied to claims 1, 19, 21 and 24, above, and further in view of US 6,129,761 to Hubbell.

Wittwer teaches gelatin or synthetic polymers that swellable and also suitable for injection molding to prepare shaped articles. Wittwer teaches natural and synthetic polymers are suitable for the preparation of injectable hydrocolloids, but fails to teach the combination with gelatin or other polymers, of instant claims.

Rothman, discussed above, teach polysaccharide swellable gels in combination with active agents or hydrocolloids comprising combinations of swellable polymers.

Hubbell teaches injectable hydrogel compositions useful for delivering cells or other bioactive agents via injection and thus provide engraftment and a 3-D template for new cell growth, custom molding of implants as well as implantation of tissues (abstract and col. 5, L 5-23) . The polymers of Hubbell include biodegradable, biocompatible hydrogels such as polylactides, polyanhydrides, polysaccharides and natural polymers such as gelatin, collagen, fibrin etc (col. 7-8), all of which described in the instant. Hubbell also teaches combination or mixtures of polymers (col. 8, L 63 –col. 9, L 12). It would have been obvious for one of an ordinary skill in the art at the time of the instant invention was made to combine other synthetic and natural swellable polymers of

Rothman or Hubbell with the polysaccharide swellable polymers of Wittwer for administration because Wittwer suggests that protein as well synthetic polymers are suitable for preparing injection moldable articles, Rothman suggests polysaccharides and Hubbell suggests several swellable hydrogel polymers (both natural polymers such as gelatin and synthetic polymers) as well as their combinations for administering active agents to the localized or for tissue remodeling or preparing shaped moldable articles. Accordingly, a skilled artisan would have expected to be able to administer active agents or promote tissue engraftment with individual as well as mixtures of hydrogel polymers.

Response to Arguments

Applicant's arguments filed 5/13/11 have been fully considered but they are not persuasive.

Applicants' arguments with respect to the Japanese patents 05308969 and 6-254148, as well as US 5,135,755 are moot because the references are no longer applied in the instant rejections.

Applicants argue that the examiner has not addressed the claimed equilibrium swell, limitation of “substantially free of free aqueous phase”, subunit sizes of the particles claimed (0.01 to 5 mm) and in vivo degradation. However, applicants previously argued the teachings of Wittwer reference (arguments 7-29-09). Applicants' arguments and the examiner's response (dated 11-25-09) are reproduced below. The examiner previously addressed the arguments regarding equilibrium swell and

degradation time. Applicants have not shown that the hydrocolloids of Wittwer do not possess the said characteristics.

"Applicants argue that it appears therefore that the obviousness rejection is based on the "obvious to try" rationale. According to this rationale, it is obvious to choose from a finite number of predictable solutions when solving a recognized problem. It is argued that Office Action does not establish that there had been a finite number of identified predictable potential solutions as required by KSR at 1397. It is argued that to the contrary, at col. 2 lines 49-60, Wittwer states that the hydrophilic polymer may be modified by crosslinking agents such as salts or tri or tetravalent metals, aldehydes, dialdehydes, halogenated aldehydes, mucochloric acid, 1,1- and 1-4 diketones, quinones, acid anhydrides, vinylsulfones, acrylamides, products with 3-membered rings such as ethyleneoxide or ethyleneimine, carbamoylonium compounds, etc., and that by such crosslinking agents the water-swellability can be varied within wide limits. Applicants' argue that Wittwer's list of crosslinking agents is admittedly incomplete by use of the term etcetera, and thus Wittwer cannot be used to establish that there were a finite number of solutions to obtain the presently claimed equilibrium swells. Moreover, assuming for the sake of argument that Wittwer did establish a finite number of solutions (which it did not), Wittwer does not establish that such a finite number of solutions were also identified and predictable solutions, as required by the "obvious to try" rationale.

It is argued that Wittwer describes a water-swellable hydrocolloid, varying water swellability with certain limits. It is argued that the absorption isotherm (fig. 1) shows water content that is 0.0 to 0.5 kg water per kg gelatin. It is argued that Wittwer does not even remotely contemplate the presently claimed equilibrium swells. As indicated in the instant application at, for example, page 18 lines 17-28, the term "equilibrium swell" can be defined as the percent swell at equilibrium, and the term "percent swell" can be defined as the dry weight subtracted from the wet weight, divided by the dry weight and multiplied by 100. According to this construction, Wittwer's maximum water content of about 0.5 involves a dry weight of 1.0kg and a wet weight of 1.5kg. Hence, Wittwer's resulting maximum percentage is ((1.5-1)/1)*(100) = 50%. Wittwer's 50% value relates to water content, but Wittwer does not mention equilibrium swell value ranges at all. Thus, it is argued that although Wittwer may discuss water content or varying the water swellability, Wittwer does not teach or suggest equilibrium swells from 400% to 5000% as presently claimed. Hence, it is argued that the artisan would not be able to produce gelatin hydrocolloid gels with the desired amount of water and obtain an even distribution of water within the granules.

Applicants' arguments are not persuasive because applicants rightly pointed out that Wittwer does suggest obtaining equilibrium swell, avoid rapid degradation and maintain water content. Even though Wittwer teaches a finite number of crosslinking agents (which may be incomplete according to applicants), the burden is on applicants to show that the finite and incomplete list of crosslinkers of Wittwer do not provide an equilibrium swell anywhere between 400% to 5000%, even though the reference

desires to provide an equilibrium swell that is variable. As explained in the previous action, Wittwer's disclosure is concerned with water-swellable hydrocolloid and particularly, the product applied for injection molding in a swellable state. Additionally, Wittwer suggests varying water swellability (col. 2, l 57-60) and also suggests obtaining particles with higher water content (col. 3, L 11). Wittwer suggests that to produce shaped articles with swellable hydrocolloids, the materials need to be plasticized and that plasticity of such water swellable colloids is a function of temperature (col. 1). Wittwer also states that swellability is also a function of the granularity and specific surface of the material and further suggests optimizing conditions of swellability so as to avoid degradation of the hydrocolloid. In this regard, instant specification on page 13, L 15-23 also states "The equilibrium swell of the cross-linked polymers of the present invention may range from 400% to 5000%, 400% to 3000%, 400% to 2000%, usually ranging from 400% to 1300%, preferably being from 500% to 1100%, depending on its intended use. Such equilibrium swell may be controlled by varying the degree of cross-linking, which in turn is achieved by varying the cross-linking conditions, such as the type of cross-linking method, duration of exposure of a cross-linking agent, concentration of a cross-linking agent, cross-linking temperature, and the like. "Thus, Wittwer similar to instant invention recognizes that swellability is a function of granularity, temperature, specific material employed etc. Wittwer is directed to solving the same problem as that of the instant invention i.e., obtain equilibrium swell, avoid rapid degradation, and maintain the water content; and also suggests finite number of possibilities that may be optimized to attain instant swellable polymer. Thus, a skilled

artisan would have been readily able to determine the conditions such as temperature, granularity, type of polymer, nature of crosslinking etc., in obtaining a hydrocolloid polymer with a predetermined amount of water, swellability and the degradation. Particularly, Wittwer suggests methods of obtaining higher quantities of water in the hydrocolloid and yet feel superficially dry such that they do not stick together (col. 3, L 1-10). The argument regarding fig. 1 is not persuasive because the teachings of the prior art are not limited to figures and examples and should be considered as a whole. One skilled in the art would be able to optimize the conditions so as to produce a hydrocolloid with desired amount of water (see claim 1 of Wittwer), even distribution of water within the granules, swellability and plasticity such that the final polymer does not degrade rapidly. For the argument regarding in vivo degradation, mere arguments without any evidence to show that the gelatin hydrocolloid gels do not degrade at the claimed rate are not persuasive".

With respect to the subunit size, instant claims recite the subunit size "when fully hydrated", which is an intended use. On the other hand, the claims have been amended to recite "partially hydrated". Thus, it is the examiner's position that instant claims only need a partially hydrated hydrocolloid and admittedly Wittwer does teach a partially hydrated colloid. With respect to the degradation time, the argument that Wittwer teaches to avoid chemical degradation is not persuasive because instant claims recite in vivo conditions with respect to the degradation time and it is the position of the examiner that if the polymers employed for the hydrocolloid is the same (gelatin in the instant case), then the in vivo degradation time is a necessary property of the polymer.

The argument regarding free aqueous phase and swellability is not persuasive because Wittwer only teaches gels for injection molding and not the addition of any suspensions or carriers for such utility".

Applicants' arguments that neither Pruss nor Cioca remedy the deficiencies of Wittwer are not persuasive because the arguments regarding Wittwer have been addressed above. Pruss and Cioca have been cited for the motivation to include an active agent in the product of Wittwer and employ the hydrocolloid gels for in vivo applications.

Applicants' argue that the teachings of Rothman do not include "a single phase or a single phase that is substantially free from free aqueous phase" because polysaccharide is in aqueous suspension that is by nature a free phase. However, instant rejection includes a combination of Wittwer, Rothman and Hubbell for the claimed combination of protein and a polysaccharide and even though Rothman teaches a suspension of polysaccharide, Wittwer teaches any hydrocolloid polymer and Hubbell teaches injectable hydrogel polymers that include mixtures of polymers. Hence, a skilled artisan would have been motivated to include a mixture of protein and polysaccharide in the hydrogel particles in the same phase and not a suspension of polysaccharide that is mixed with gelatin hydrogel.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAKSHMI CHANNAVAJJALA whose telephone number is (571)272-0591. The examiner can normally be reached on 9.00 AM -5.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lakshmi S Channavajjala/
Primary Examiner, Art Unit 1611